Coffee Drinking and Risk of Bladder Cancer[1,2,3]

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ABSTRACT—The relationship between coffee drinking and risk of bladder cancer was assessed with the use of data from a case-control study of bladder cancer. Incident cases (2,982) and general population controls (5,782) were interviewed. Overall, the relative risk (RR) of bladder cancer for subjects who had ever drunk coffee was estimated as 1.4 (95% confidence interval=1.1-1.8). There was no consistent relation between the RR estimate and the current consumption level. Among men who drank coffee, those who drank more than 49 cupfuls of coffee per week had an apparent excess in risk, but women who drank that much had an apparent deficit in risk.—JNCI 1983; 70:1021-1026.

In 1971, a report from a case-control study of bladder cancer (*1*) suggested that coffee might cause human bladder cancer. Several but not all subsequent studies have reported an association among men; fewer studies have reported an association among women (*2-12*). The inconsistencies in the data and the apparent lack of a dose response in most studies suggest that coffee drinkers may be at increased risk of bladder cancer but that coffee drinking itself may not cause bladder cancer. Nonetheless, concern about coffee has not been entirely laid to rest, partly because brewed coffee has shown mutagenic activity (*13*) and because caffeine, coffee's principal active constituent, alters susceptibility of various organisms to mutation by other agents (*14-17*). We therefore evaluated the relation between coffee and bladder cancer using interview data from a large case-control study.

METHODS

We interviewed 2,982 cases and 5,782 controls as part of a collaborative population-based case-control study conducted in 10 geographic areas of the United States—Atlanta, Ga.; Connecticut; Detroit, Mich.; Iowa; New Jersey; New Mexico; New Orleans, La.; San Francisco, Calif.; Seattle, Wash.; and Utah (*18*). The case group was composed of all identified residents of the areas who were of ages 21-84 years and who were diagnosed with histologically confirmed bladder cancer in a 1-year period (with the beginning varying among areas from December 1977 to March 1978). Cases were identified from cancer registries, nine of which were part of the Surveillance, Epidemiology, and End Results Program of the National Cancer Institute. The control group was randomly selected from the general population (weighted by the age, sex, and geographic distribution of the cases). Controls aged 21-64 years were selected from 22,633 households chosen by telephone sampling with the use of random-digit dialing (*19*). Controls aged 65-84 years were selected from Health Care Financing Administration rosters.

We identified 4,086 eligible cases and interviewed 2,982 (73%) of them. The remaining 1,104 were not interviewed because of death (282), illness (288), patient refusal (252), physician refusal (128), being identified after the study ended (65), not being found (81), and other reasons (8). A total of 4,057 older controls were eligible, of whom 3,313 (82%) were interviewed. The remaining 744 were not interviewed because of death (94), illness (174), refusal (348), not being found (105), and other reasons (23). From telephone sampling of households, 2,928 people younger than 65 were selected as controls, of whom 2,469 (84%) were interviewed. The remaining 459 were not interviewed because of death (7), illness (23), refusals (335), not being found (87), and other reasons (7). About 75% of the interviewed cases (and controls) were male, and the median age was 67 years.

All subjects were interviewed at home. Interviewers used a questionnaire that included questions about the use of artificial sweeteners, hair dyes, and tobacco products, occupational history, and residential history. In addition, a brief series of questions was asked about each of several other exposures, including exposures to coffee and tea. Respondents were asked whether they had drunk more than 100 cupfuls of coffee in their life ("coffee drinkers") and, if so, how many years they had drunk coffee. For the measurement of recent or "current," prediagnosis coffee consumption, respondents were asked how many cupfuls of various types of coffee (e.g., ground decaffeinated) they typically drank each week in the winter 1 year ago (i.e., before onset of the cases' illness).

The effect of coffee drinking on bladder cancer risk was measured by the maximum likelihood estimate of the RR, controlled for potentially confounding variables by stratification into multiple contingency tables and by entering continuous variables into multiple logistic regression models (*20, 21*).

The estimates are presented separately for males and females. They were adjusted for age (21-44, 45-64, and 65-84 yr), race (white or other), residence (the 10 study areas), and tobacco smoking history (nonsmokers, smokers of pipes or cigars only, ex-smokers of <20 cigarettes/day, ex-smokers of ≥20 cigarettes/day, smokers of <20 cigarettes/day, smokers of 20-39 cigarettes/day, and smokers of ≥40 cigarettes/

ABBREVIATIONS USED: CI=confidence interval; RR=relative risk(s).

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[3] Research procedures were in accord with the ethical standards of the human subjects' investigation committees of each participating hospital and registry.

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day). Exceptions are noted in the text. Finer adjustment for amount smoked did not affect the estimates of RR, nor did control for other indices of tobacco exposure. These indices included the usual numbers of filtered cigarettes and unfiltered cigarettes separately, the usual number of cigars or pipes, the lifetime number of packs smoked, the number of years since quitting smoking, the number of years of smoking, and combinations of these variables. The estimates were also not appreciably altered by finer adjustment for age or by adjustment for urinary stones or infections, hair dyeing, fluid intake, artificial sweetener use, urban residence, usual occupation, exposure to suspect chemicals (dye, rubber, leather, ink, or paint), or religion.

RESULTS

Six percent of the subjects in the control group said that they had drunk fewer than 100 cupfuls of coffee in their lives ("nondrinkers"). The coffee drinkers reported consuming 11.8 cupfuls per week of regular (nondecaffeinated) ground coffee, on average. They reported substantially lower consumption of regular instant coffee (5.3 cupfuls/wk), decaffeinated instant coffee (3.2), decaffeinated ground coffee (0.8), coffee with chicory (0.6), and espresso (0.1). All types of coffee were combined to estimate total current consumption, and the four caffeine-containing types were combined to estimate current consumption of caffeinated coffee. Coffee consumption patterns varied with sex, race, age, and tobacco consumption (table 1).

TABLE 1.—*Patterns of coffee consumption within general population control group*

Variables	Percent ever drank coffee	Mean weekly cups of coffee among drinkers
Sex		
Male	94	22
Female	92	20
Age, yr		
21–44	83	24
45–64	94	26
65–84	94	19
Race		
White	94	22
Other	87	15
Area[a]		
Atlanta, Ga.	95	19
Connecticut	95	19
Detroit, Mich.	95	24
Iowa	91	26
New Jersey	95	19
New Mexico	94	23
New Orleans, La.	94	22
San Francisco, Calif.	96	22
Seattle, Wash.	96	27
Utah	72	19
Cigarettes[a]		
Never smoked	88	17
Former smokers, <1 pack/day	95	19
Former smokers, ≥1 pack/day	97	22
Current smokers, <1 pack/day	96	22
Current smokers, ≥1 pack/day	96	28
Job exposure[a]		
Never handled dye, rubber, leather, ink, or paint	94	21
Handled dye, rubber, leather, ink, or paint	93	22
Artificial sweeteners[a]		
Never used	93	22
Used <240 mg/day	95	22
Used ≥240 mg/day	92	25

[a] Standardized to the age, sex, and race distribution of the entire control group.

All Coffees

Table 2 shows the estimated RR of bladder cancer according to history of coffee drinking for men and women separately and for both sexes combined. The overall RR estimate, adjusted only for sex, age, race, and area of residence, was 1.8 for drinkers versus nondrinkers, but this estimate was markedly confounded by the effect of smoking, and the adjusted estimate was 1.4 (95% CI=1.1–1.8). The estimated effect was greater in men than women, but the difference was not statistically significant (P=0.39).

Table 3 presents the RR estimated according to duration of coffee drinking. Study subjects who never drank coffee were not included. RR did not vary appreciably according to duration of coffee drinking. As table 4 shows, current drinkers had substantially the same risk as former drinkers.

Table 5 presents RR estimates according to current level of consumption of all types of coffee combined. Because ex-drinkers had the same adjusted RR as current light drinkers, they were combined to form the group of lowest exposure (0–7 current cupfuls/wk) to which all other groups were compared. Among men, RR appeared to be constant for levels up to 49 cupfuls per week, but it was slightly elevated at the highest level (>49 cupfuls/wk). The 87 men who reported more than 84 weekly cupfuls showed an RR of 1.5. Among women, a slight deficit in RR appeared for all levels above 0–7 cupfuls per week, with no evidence of a trend.

We estimated the simultaneous effects of a history of coffee drinking (yes/no), duration of coffee drinking (yr), and current consumption (cupfuls/day) using a logistic regression to adjust for age in 5 groups, sex, race, geographic area in 2 groups, and tobacco history in 7 groups. Among men, the RR for ever drinking versus never drinking was estimated as 1.3 (95% CI=0.9–1.9), the estimated multiplication of RR for each year of coffee drinking was 1.00 (95% CI=1.00–1.01), and the estimated multiplication of RR for

TABLE 2.—*Estimated RR of bladder cancer according to history of coffee drinking, by sex*

Sex	Coffee	No. of cases	No. of controls	RR[a]	95% CI
Male	Never drank	58	244	1.0	
	Ever drank	2,139	3,942	1.6	1.2–2.2
Female	Never drank	40	121	1.0	
	Ever drank	670	1,347	1.2	0.8–1.7
Both sexes	Never drank	98	365	1.0	
	Ever drank	2,809	5,289	1.4	1.1–1.8

[a] RR estimates are from a logistic regression model including (sex), age, race, geographic area, and tobacco history.

TABLE 3.—*Estimated RR of bladder cancer among coffee drinkers according to duration of coffee drinking, by sex*

Duration of coffee drinking, yr	Males				Females			
	No. of cases	No. of controls	RR[a]	95% CI	No. of cases	No. of controls	RR[a]	95% CI
<10	32	88	1.0		17	30	1.0	
10–19	55	147	0.9	0.5–1.5	28	65	0.8	0.4–1.7
20–39	462	875	1.1	0.7–1.6	164	322	0.8	0.4–1.6
≥40	1,565	2,781	1.1	0.7–1.6	456	911	0.8	0.4–1.5
(Unknown)	(25)	(51)			(5)	(19)		

[a] RR estimates are from a logistic regression model including age, race, geographic area, and tobacco history.

TABLE 4.—*Estimated RR of bladder cancer among coffee drinkers according to whether drinking recently, by sex*

Recent coffee	Males				Females			
	No. of cases	No. of controls	RR[a]	95% CI	No. of cases	No. of controls	RR[a]	95% CI
Ex-drinker	91	205	1.0		37	73	1.0	
Recent drinker	2,021	3,687	1.1	0.8–1.4	627	1,263	1.0	0.6–1.5
(Unknown)	(27)	(50)			(6)	(11)		

[a] RR estimates are from a logistic regression model including age, race, geographic area, and tobacco history.

TABLE 5.—*Estimated RR of bladder cancer according to recent cupfuls of coffee per week among coffee drinkers, by sex*

Cupfuls of coffee per week	Males				Females			
	No. of cases	No. of controls	RR[a]	95% CI	No. of cases	No. of controls	RR[a]	95% CI
≤7	397	862	1.0		164	331	1.0	
7.1–14	389	842	0.9	0.8–1.1	161	346	0.9	0.7–1.2
14.1–21	381	747	1.0	0.8–1.2	110	237	0.8	0.6–1.1
21.1–35	493	821	1.1	0.9–1.3	133	249	0.9	0.7–1.2
35.1–49	195	329	1.0	0.8–1.3	49	104	0.7	0.5–1.1
49.1–63	109	139	1.2	0.9–1.6	21	31	0.9	0.5–1.7
63.1–155	148	152	1.5	1.1–1.9	26	38	0.8	0.4–1.4
(Unknown)	(27)	(50)			(6)	(11)		

[a] RR estimates are from a logistic regression model including age, race, geographic area, and tobacco history.

each cupful per day currently drunk was 1.04 (95% CI=1.01–1.06). Among women, the corresponding estimates were 1.2 (95% CI=0.7–1.9) for ever drinking, 1.00 (95% CI=0.99–1.01) for each year of drinking, and 0.99 (95% CI=0.94–1.03) for each current cupful per day.

Caffeine

When only caffeine-containing coffees were combined, the pattern observed in table 5 among men was virtually unaffected. Among women, those who consumed at the highest level showed a slightly elevated RR, but there was no evidence of a trend. The slight excess RR associated with a history of coffee drinking was not attributable to any particular type of coffee consumed, nor was the slight additional excess RR to men who drank more than 49 cupfuls per week.

Compared to men who never drank any type of coffee, men who were drinking only decaffeinated coffee (ground or instant) had an estimated RR of 1.2 (95% CI=0.8–1.9). The corresponding estimate for women was 1.5 (95% CI=0.9–2.6). Among men who drank only decaffeinated coffee, those who drank more than 49 cupfuls per week showed the highest RR, but there was no consistent relation between the amount of coffee and RR. Among women who drank only decaffeinated coffee, there was also no consistent relation between RR and the amount of coffee, but those who drank most heavily showed the lowest RR. Essentially similar patterns appeared when all of the subjects were included in the analysis and the estimates were adjusted for the effects of consumption of caffeine-containing coffee.

Although 90% of caffeine ingested in the United States comes from coffee (*22*), some people consume a substantial amount of caffeine from tea and drink little or no coffee. On average, a cupful of tea contains about 60 mg of caffeine, whereas a cupful of coffee contains about 90 mg (*22*). Among subjects who were currently drinking no more than 7 cupfuls of coffee per week, tea consumption was weakly and inconsistently related to RR of bladder cancer (table 6). In the total study group, tea consumption was weakly related to RR. Women who drank more than 7 cupfuls per week had slightly elevated RR (RR=1.2 for 7.1–14 cupfuls; RR=1.3 for >14 cupfuls). Men who drank more than 14 cupfuls per week had a slightly elevated RR (RR=1.2).

TABLE 6.—*Estimated RR of bladder cancer according to recent consumption of tea among subjects who drank no more than 7 cupfuls of coffee per week, by sex*

Recent tea—cupfuls per week	Males				Females			
	No. of cases	No. of controls	RR[a]	95% CI	No. of cases	No. of controls	RR[a]	95% CI
0	198	510	1.0		56	163	1.0	
0.1–7	137	322	1.1	0.8–1.4	63	150	1.1	0.7–1.7
7.1–14	59	132	1.1	0.7–1.5	40	57	1.7	1.0–2.9
>14	59	140	1.0	0.7–1.4	44	81	1.2	0.7–2.0
(Unknown)	(2)	(2)			(1)	(1)		

[a] RR estimates are from a logistic regression model including age, race, geographic area, tobacco history, and history of coffee drinking.

TABLE 7.—*Estimated effects of ever drinking coffee and of heavy recent consumption, by sex and tobacco history*

Sex	Tobacco	Ever vs. never[a]			>49 cupfuls/wk vs. less cupfuls[a]		
		No. of subjects who never drank	RR[b]	95% CI	No. of subjects who drank >49 cupfuls/wk	RR[b]	95% CI
Both sexes	All	463	1.4	1.1–1.8	664	1.3	1.1–1.5
Male	All	302	1.6	1.2–2.1	548	1.3	1.1–1.6
Female	All	161	1.2	0.8–1.7	116	1.0	0.7–1.5
Male	Nonsmokers	159	1.5	0.9–2.5	21	4.2	1.7–10.
	Pipes, cigars only	25	2.2	0.6–7.8	17	0.8	0.3–2.7
	Ex-smokers	62	1.4	0.8–2.6	208	1.3	1.0–1.8
	Smokers	56	2.1	1.2–3.9	302	1.2	1.0–1.6
Female	Nonsmokers	121	0.9	0.6–1.5	24	0.4	0.1–1.5
	Ex-smokers	13	3.0	0.8–12.	25	1.7	0.7–4.2
	Smokers	27	1.3	0.6–2.9	67	1.0	0.6–1.7

[a] Subjects who drank >49 cupfuls/wk are compared to all others who ever drank.
[b] RR estimates are from separate logistic regression models with terms for sex, age, race, and amount of tobacco.

TABLE 8.—*Estimated effects of ever drinking coffee and of heavy recent consumption, by sex and geographic area*

Sex	Area	Ever vs. never[a]			>49 cupfuls/wk vs. less cupfuls[a]		
		No. of subjects who never drank	RR[b]	95% CI	No. of subjects who drank >49 cupfuls/wk	RR[b]	95% CI
Male	Atlanta, Ga.	11	—	—	16	1.2	0.4–3.8
	Connecticut	29	3.2	0.9–11.	49	1.6	0.9–2.6
	Detroit, Mich.	27	1.1	0.4–2.6	69	1.1	0.6–1.8
	Iowa	34	2.2	0.8–5.8	95	1.3	0.8–2.1
	New Jersey	74	2.1	1.1–3.9	121	1.3	0.9–2.0
	New Mexico	8	0.7	0.1–4.1	25	3.2	1.1–9.5
	New Orleans, La.	14	0.8	0.2–3.0	14	0.9	0.3–3.0
	San Francisco, Calif.	30	1.4	0.6–3.6	75	1.3	0.8–2.2
	Seattle, Wash.	12	0.3	0.1–1.4	56	1.0	0.5–1.8
	Utah	63	1.5	0.7–3.5	28	2.3	0.9–5.8
Female	Atlanta, Ga.	6	0.7	0.1–8.0	3	[c]	
	Connecticut	18	1.8	0.6–5.6	15	1.5	0.5–4.7
	Detroit, Mich.	17	1.2	0.4–3.6	13	1.2	0.4–4.0
	Iowa	18	2.2	0.5–11.	31	0.8	0.3–2.1
	New Jersey	37	1.0	0.5–2.2	19	0.6	0.2–1.6
	New Mexico	4	[c]		2	[c]	
	New Orleans, La.	3	[c]		2	[c]	
	San Francisco, Calif.	17	0.9	0.3–2.8	17	2.6	0.8–8.5
	Seattle, Wash.	3	[c]		11	0.5	0.1–2.6
	Utah	38	0.5	0.2–1.7	3	[c]	

[a] Subjects who drank >49 cupfuls weekly are compared to all others who ever drank.
[b] RR estimates are from separate logistic regression models including age, race, and tobacco history.
[c] Fewer than 5 subjects exposed or fewer than 5 subjects unexposed.

Subgroups

The data in tables 2–5 show three discrete levels of RR for men (nondrinkers, very heavy drinkers, and all others) and two levels for women (nondrinkers and drinkers). To examine how the effects of coffee varied within subgroups, we considered two contrasts: subjects who ever drank versus those who never drank and subjects who drank very heavily versus all others who ever drank (tables 7, 8). The RR estimates for ever drinking coffee, within the seven tobacco history categories, did not show statistically significant heterogeneity (P=0.81), but the nonsmokers had estimates different from those for the smokers. The estimates for current smokers and for ex-smokers did not depend on the usual amount smoked, so we combined categories and adjusted for the amount smoked. Estimated RR for ever drinking coffee was lower among women and nonsmokers. Excess RR for heavy coffee drinking was absent among women, but it was present among nonsmokers.

Although estimates of RR varied by geographic area, the pattern seen overall was not confined to one area or region. For both sexes combined, the geographic variation was no more than would be expected by chance (P=0.44). The estimated RR for ever drinking also did not vary significantly by race (P=0.43), usual occupation (P=0.65), artificial sweetener use (P=0.18), history of urinary infection (P=0.86), or source of controls (P=0.85).

DISCUSSION

Our data show coffee drinkers to be at apparently greater risk of bladder cancer than nondrinkers, but the data do not show any consistent relationship between the extent of exposure and the degree of risk. We estimated that current and former coffee drinkers had an RR of bladder cancer of 1.4 compared to nondrinkers. Among subjects who never smoked, the estimate was 1.2. We found no consistent pattern of higher RR with higher levels of current coffee consumption. Although men who drank more than 49 cupfuls of coffee per week showed a slightly elevated risk, those who drank 35.1–49 cupfuls of coffee per week showed no elevation. Further, women who drank coffee heavily showed RR below the null value. The number of years that subjects had drunk coffee was apparently unrelated to RR. The patterns of RR within subgroups did not suggest a consistent pattern of interaction with other risk factors for bladder cancer.

Our findings are consistent with findings from earlier epidemiologic studies, many of which have reported slightly and inconsistently elevated risks of bladder cancer among coffee drinkers. Two case-control studies similar in design to the present study have recently been reported. A study by Howe et al. (*10*) conducted in three Canadian provinces estimated the RR to coffee drinkers as 1.4 (95% CI=0.9–2.0) among males and 1.0 (95% CI=0.5–2.1) among females, with no evidence of a dose response. A study by Morrison et al. (*12*) conducted in Boston, Mass., Nagoya, Japan, and Manchester, England, estimated the RR as 1.0 (95% CI=0.8–1.2) for both sexes combined, with no evidence of a dose response.

Like the epidemiologic evidence, the laboratory evidence about the possible carcinogenic effects of coffee does not lead to a definite conclusion. It is well established that caffeine can enhance the effects of some mutagens and inhibit the effects of others in a variety of bacterial systems and cell cultures (*14–17*). The tests of direct effects of caffeine in such systems have been predominantly negative, but positive results have been reported from Ames assays of whole brewed coffee but not of caffeine (*13*). Tests of coffee or caffeine in animals pretreated with known carcinogens showed that the coffee or caffeine either decreased (*23*) or did not alter (*24*) tumor yield. To date, the whole-animal tests of caffeine alone have not shown that caffeine is carcinogenic (*25–27*). A standard National Cancer Institute bioassay of caffeine is under way and will be completed in late 1983. In short, the existing laboratory evidence does not suggest that coffee is likely to be a powerful human carcinogen, but it does suggest two possible mechanisms by which coffee might influence cancer risk, i.e., by the mutagenic action of coffee or by the interaction of caffeine with some other mutagen.

There are several possible interpretations of the current evidence. The patterns observed in this study may be due to a noncausal association between coffee drinking and bladder cancer, to a causal relation, or to chance. Chance is the least likely explanation, in view of the large size of this study and the replication of the finding of a low-level association in many studies.

If the association is causal, one would expect to observe a relation between risk and duration or dose. Our study, like other studies, showed no such relation. It is possible, but not likely, that drinking even modest amounts of coffee for a short period of time raises the risk of bladder cancer, while greater exposure does not further raise the risk, except perhaps at the very extreme. A second possible interpretation is that greater coffee consumption does lead to greater RR but that our dose data were so severely misclassified that the dose-response relation was obscured.

Two possible explanations of a noncausal relation are residual confounding by tobacco and confounding by other correlates of coffee drinking. (Other noncausal interpretations of our findings are also possible, but less likely, in our view. For example, if coffee drinking increased chances of survival from bladder cancer, then the cases available for interview would have had a higher exposure rate than the case group as a whole.)

Confounding by tobacco was present in these data because tobacco is a strong risk factor for bladder cancer and is highly correlated with amount of coffee drunk, in part because caffeine clearance rates are about twice as high in smokers as in nonsmokers (*28*). Adjustment for smoking markedly reduced the estimated RR—from 1.8 to 1.4. Despite our adjustments, residual confounding could have occurred through 1) insufficiently narrow categories of tobacco exposure in the multiple contingency table analysis, 2) misspecification of the analytic models, or 3) random errors (misclassification) in the tobacco data. To reduce the possibility of the first two problems, we examined a wide variety of tobacco exposure indices and analytic models and tried very narrow categories of tobacco exposure. Residual

confounding because of misclassification of tobacco was present to the extent that study subjects did not perfectly recall and report tobacco histories. With a sample of respondents, we conducted a brief telephone re-interview. There was 97% concordance between the history of nonfilter smoking (yes or no) reported in the re-interview and that reported in the original home interview. We do not know whether the more complicated tobacco questions would have shown high accordance, and we do not know if the answers were accurate as well as replicable. Greenland (*29*) discussed the problem of misclassification of covariates leading to residual confounding, and Morrison et al. (*12*) and Morrison (paper presented at the annual meeting of the Society for Epidemiologic Research) discussed the particular implications for coffee, tobacco, and bladder cancer. Whether residual confounding accounts for the entire observed excess RR of 40% cannot be determined.

Confounding by correlates of coffee drinking other than tobacco exposure may also have contributed to the persistent but inconsistent relation between bladder cancer and coffee. As noted, control for a variety of factors did not materially alter the estimates. Overall, people who never drank coffee are a small minority of American adults, and the distinguishing characteristics of this minority are not well understood. They may differ from coffee drinkers on a variety of health-related variables, but it is not clear what other correlates of coffee drinking might be related to bladder cancer.

Further studies of typical U.S. populations are not likely to provide more precise estimates than those from this unusually large study, and they are not likely to avoid the bias created by residual confounding by tobacco. Additional studies of populations with a low prevalence of coffee drinking, e.g., Mormons or Seventh-Day Adventists, may illuminate the comparison of nondrinkers and drinkers. (We are pursuing this possibility by continuing the present study in Utah.) Studies of populations who drink more coffee than the U.S. population, e.g., Scandinavians, may also reveal whether very high doses of coffee affect bladder cancer risk. In addition, the completion of laboratory tests in progress will further our understanding of the effects of coffee. Meanwhile, the available evidence from our study, other epidemiologic studies, and laboratory experiments suggests that coffee plays either a small biologic role in human bladder cancer or no role at all.

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